105. The method of Claim 86, wherein the oocyte is enucleated by microsurgical methods.

106. The method of Claim 86, wherein the oocyte is enucleated about 10 to 40 hours after initiation of *in vitro* maturation.

107. The method of Claim 86, wherein the oocyte is matured *in vivo* prior to enucleation.

108. The method of Claim 86, wherein the non-human mammal is bovine.

109. The method of Claim 86, wherein the non-human mammal is bovine.--

REMARKS:

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks which follow, are respectfully requested.

By the present amendment, current Claims 1 through 85 have been cancelled in favor of new Claims 86 through 109. Claims 1-85 have been cancelled in order to expedite prosecution. Essentially, the newly-submitted claims substantially correspond to the claims previously allowed by the Examiner in U.S. Serial No. 08/ 781,752, now

U.S. Patent 5,945,577, except for the fact that the donor cell is recited to be a proliferating somatic cell rather than a proliferating somatic cell that has been expanded in culture. Such amendment finds support in the as-filed disclosure, especially the Examples which disclose the use of a donor cell which is a proliferating somatic cell.

Turning now to the Office Action, Applicants note that all of the elected claims stand rejected. This rejection is respectfully traversed to the extent they may be applicable to the claims as amended herein.

Previous Claims 1 to 19, 26, 27, 31 and 34, 36, 38, 50-52, 54, 56, 58, 59, 61, 63, 65-69, 84 and 85 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 103 to 126 of allowed U.S. Application Serial No. 08/781,752, now USP 5,945,577. The Examiner is respectfully requested to hold this rejection in abeyance until this application is otherwise in condition for allowance.

Also, Claims 1-19, 26, 27, 31-34, 36, 38, 50-52, 54, 56, 58, 59, 61, 63, 65-69, and 84-89 were rejected under 35 U.S.C. §112, first paragraph, as assertedly being broader than the enabling disclosure. Applicants note that a similar rejection was made in U.S. Serial No. 08/781,752, which rejection was effectively overcome by submission of a §132 Declaration by Dr. Robl, an inventor of this application. For the convenience of the Examiner, a copy of this Declaration is attached to this Reply. As the claims are substantially identical to the previously allowed claims, this Declaration should be sufficient to overcome this rejection. Moreover, the recitation that the donor cell is a

proliferating somatic cell rather than a proliferating somatic cell that has been expanded in culture, should not raise any new §112 enablement issues. Essentially, this Declaration provides convincing evidence that a proliferating somatic cell may be used as an effective donor, i.e., one which gives rise to a viable, cloned, non-human mammal when utilized as a nuclear transfer donor. Applicants note that the previous allowed claims were unnecessarily limited to cells which had been expanded in culture. Such a limitation was not necessary to overcome the enablement rejection and, moreover, is not necessary to overcome any potential rejection based on cloning procedures that use quiescent donor cells, such as the nuclear transfer procedures reported by Ian Wilmut of the Roslin Institute. Rather, as argued during prosecution of U.S. Serial No. 08/781,752, Roslin makes quite clear that their procedures are limited to the use of donor cells which are serum-starved, i.e., which are quiescent and, therefore, are not proliferating. By contrast, all of the current claims require that the donor cell is a proliferating somatic cell, or a nucleus derived from a proliferating somatic cell. Such a nuclear transfer procedure is not suggested by any prior art reference known to Applicants.

Moreover, Applicants respectfully advise that a proliferating somatic cell has been introduced so as to cover proliferating donor cells obtained, e.g., from adult animals. In this regard, as demonstrated in the §132 Declaration, the use of adult donor cells as effector nuclear transfer donor cells has been reported. Moreover, there is no requirement that such a cell be cultured prior to nuclear transfer. In fact, as argued and previously demonstrated during prosecution of the earlier application, the novelty of the claimed

invention involves the surprising discovery that a proliferating somatic cell or a nucleus derived therefrom may be used as a nuclear transfer donor in order to produce a cloned, non-human mammal or fetus. Therefore, based on arguments submitted in Applicants' prior application, and the §132 Declaration attached hereto, withdrawal of the §112 enablement rejection is respectfully believed to be in order.

Also, various claims were rejected under 35 U.S.C. §112, second paragraph, as assertedly being indefinite. This rejection is not addressed herein as this rejection should be moot in light of the present claim amendments.

Previous Claims 20-22, 60, 70, 71, 77 and 81 were rejected under 35 U.S.C. §102(b) as assertedly being anticipated by USP 5,057,420. This rejection is moot in light of the present amendments.

Further, Claims 23-25, 28-30, 53, 55, 57, 62, 64, 78, 79, 80 and 82 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Hyttinen et al. This rejection is also moot in light of the present amendments.

Also, Claim 35 was rejected under 35 U.S.C. §102(b) as assertedly being anticipated by Sims et al (1993). Similarly, this rejection is moot in light of the present claim amendments.

Claim 39 was rejected under 35 U.S.C. §102(b) as assertedly being anticipated by Donkin et al (1993). This rejection is also moot in light of the present claim amendments.

Finally, Claim 37 was rejected under 35 U.S.C. §103(a) as assertedly being unpatentable over Sims et al (1993) in view of Lovell-Badge et al (1985). This rejection is not addressed herein as it is moot in light of the present claim amendments.

Based on the foregoing, this application is believed to be in condition for allowance, especially because the claims substantially correspond to those previously allowed in the parent application, except for the deletion of the recitation that the proliferating somatic cell has been expanded in culture. As argued, *supra*, such limitation is not necessary in order to distinguish any prior art known to Applicants. Moreover, such limitation is not essential to the efficacy of the subject invention, especially based on arguments and evidence contained in the §132 Declaration by Dr. Robl, which substantiates that the novelty of the claimed nuclear transfer procedure does not hinge upon any culturing procedure. Rather, it is based on the generic discovery that a proliferating somatic cell is a suitable donor for nuclear transfer for the production of a desired cloned, non-human mammal, which optionally may be transgenic. Such generic discovery could not have been reasonably predicted based on the state of the prior art relating to nuclear transfer which would have reasonably suggested that only embryonic cells were suitable donors for nuclear transfer.

Therefore, based on the foregoing, withdrawal of the outstanding rejections and allowance of this application is respectfully believed to be in order. A Notice to that effect is respectfully solicited. If the Examiner has any questions relating to this

Response, or any other matter, she is respectfully requested to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

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